This guidance document is used to determine whether the consent process can be waived for non-exempt emergency Human Research

### 1. Emergency research consent waiver

**21 CFR §50.24 and 45 CFR §46 Waiver of informed consent requirements in certain emergency research**

1.1 The subjects are in a life-threatening situation

1.2 Available treatments (see Footnote 1) are unproven (see Footnote 2) or unsatisfactory (see Footnote 3)

1.3 The collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions

1.4 Obtaining informed consent is not feasible because all of the following are true:
   - The subjects will not be able to give their informed consent as a result of their medical condition
   - The intervention must be administered before consent from the subjects’ LARs is feasible
   - There is no reasonable way to identify prospectively the individuals likely to become eligible for participation

1.5 Participation in the research holds out the prospect of direct benefit to the subjects because all of the following are true: (see Footnote 4)
   - Subjects are facing a life-threatening situation that necessitates intervention
   - Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects
   - Risks are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity

1.6 The research could not practicably be carried out without the waiver (see Footnote 5)

1.7 An independent data monitoring committee will oversee the research

1.8 Additional protections of the rights and welfare of the subjects will be provided, including:
   - Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research will be conducted and from which the subjects will be drawn (see Footnotes 6 and 7)
   - Public disclosure to the communities in which the research will be conducted and from which the subjects will be drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits (see Footnote 8)
   - Public disclosure of sufficient information following completion of the research to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results (see Footnote 9)

1.9 The IRB has considered the concerns and objections raised during community consultation activities (see Footnote 10)

1.10 The proposed research defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact an LAR for each subject within that window of time and, if feasible, to asking the LAR contacted for consent within that window rather than proceeding without consent

1.11 The investigator will summarize efforts made to contact LARs and make this information available to the IRB at the time of continuing review

1.12 The IRB has reviewed and approved consent procedures and a consent document in accord with 45 CFR 46.116 and 46.117. These procedures and the consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documented is feasible. In addition, the IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject’s participation in the research consistent with the paragraph of this waiver.

1.13 If obtaining informed consent is not feasible and an LAR is not reasonably available, the investigator has committed, if feasible, to attempt to contact within the therapeutic window the subject’s family member (see Footnote 11) who is not an LAR, and asking whether he or she objects to the subject’s participation in the research when feasible

1.14 The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review

1.15 Procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, LAR of the subject, or if such LAR is not reasonably available, a family member, of the subject’s inclusion in the research, the details of the research and other information contained in the informed consent document
| 1.16 | There is a procedure to inform the subject, or if the subject remains incapacitated, LAR of the subject, or if such LAR is not reasonably available, a family member, that he or she may discontinue the subject’s participation at any time without penalty or loss of benefits to which the subject is otherwise entitled |
| 1.17 | If an LAR or family member is told about the research and the subject’s condition improves, the subject is also to be informed as soon as feasible |
| 1.18 | If a subject is entered into research with waived consent and the subject dies before an LAR or family member can be contacted, information about the research is to be provided to the subject’s LAR or family member, if feasible |
| 1.19 | A licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation concurs with the above findings |

2. **FDA-regulated emergency research consent waiver** 21 CFR §50.24
   - The protocol is performed under a separate IND or IDE that clearly identifies such protocols as protocols that may include subjects who are unable to consent (see Footnote 12)

3. **HHS-regulated emergency research consent waiver** 45 CFR §46 Waiver of informed consent requirements in certain emergency research
   - The research does not involve "Prisoners" as subjects
   - The research does not involve "Fetuses", "Pregnant Women", and human in vitro fertilization
   - One of the following is true:
     - The research is FDA-regulated and meets the above requirements of 21 CFR §50.24
     - The research is not FDA-regulated and meets the above requirements of the 45 CFR §46 Waiver of informed consent requirements in certain emergency research

4. Research regulated by a Federal department or agency other than HHS or FDA
   - The applicable department or agency Secretary has issued a waiver

5. Notes

6. Footnotes

   6.1 FDA has interpreted the term “available therapy” to mean therapy that is specified in the approved labeling of regulated products, with only rare exceptions. For example, a treatment that is not FDA-regulated (e.g., surgery) or a drug that is not labeled for a specific use but which is nevertheless supported by compelling evidence in the medical literature may be considered an “available treatment.” The IRB should consider: What is the current “standard of care”? What treatments are available? Are available treatments (including standard of care treatments) “unproved”? If a product is not approved, but widely used, could a study be done to support approval? Are available treatments unsatisfactory, and if so, how? Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research

   6.2 In general, “unproved” means that there is not substantial evidence that a treatment is effective for the condition of interest. This may reflect the absence of any data or the absence of studies of acceptable quality. The term “unproved therapy” includes: Treatment that is considered “standard of care” but which has never been subjected to rigorous scientific testing or submitted to FDA for approval; Treatment for which there are no or insufficient clinical or pre-clinical data to support safety or efficacy of the product; Treatment for which existing studies and data are insufficient to serve as the basis of approval even if the data were submitted to FDA; A product that is not approved for, nor does the labeling for the product contain, the specific indication under study; and an available product or therapy that is not labeled for use in a specific patient population (e.g., pediatric use). Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research

   6.3 Although a treatment may be “approved” and “available,” it may be unsatisfactory. “Unsatisfactory” includes situations in which the available product or therapy is effective, but there are other drawbacks to its use, such as: Safety issues (e.g., high incidence of adverse effects; exacerbation of an adverse effect for the relevant subject population); Efficacy issues, including: Poor survival rate; The treatment is only partially effective; The treatment fails to prevent a significant permanent disability; Established efficacy is low; The time for the treatment to be effective is too long (e.g., time to cessation of seizures); The treatment has limitations related to the setting in which it is needed (e.g., should be administered in the field but needs refrigeration); is not portable; may be difficult to use (must be administered intravenously, requires surgical intervention) Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research

   6.4 The information from animal and preclinical studies, other clinical data (e.g., use of the product in another setting or for another diagnosis or in a different study population) or other evidence should support the potential for the investigational product to provide a direct benefit to the individual subjects. Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research

   6.5 If the results obtained in consenting subjects could be generalized to subjects who are unable to provide consent, or the research would not be unduly delayed by restricting it to consenting subjects, then FDA would expect the research to be performed in consenting subjects. Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research

   6.6 The IRB must review the plans for community consultation and public disclosure before the plans are implemented. The IRB should assess whether the community consultation plans adequately provide for reaching the community from which subjects will be drawn. Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research
At a minimum, the content of community consultation should include:

- A summary of the research protocol, study design, and a description of the procedures to be followed, including the identification of any procedures which are experimental;
- A summary of other available treatment options and what is known about their risks and benefits;
- An estimate of how long the study will last and expected duration of the subject’s participation;
- How potential study subjects will be identified;
- Information about the test article’s use, including a balanced description of the risks and expected benefits and any relevant information that is known about adverse events;
- A clear statement that informed consent will not be obtained for most research subjects;
- The rationale as to why the study must be conducted using an exception from informed consent;
- Relevant information that would be part of the informed consent process, e.g., available treatments for the condition under study; risks/potential benefits of participating in the research; possibility that FDA might inspect the subject’s records;
- A description of the therapeutic window, during which the test article must administered, and the portion of that window that will be used to contact the subject’s LAR;
- A description of the attempts that will be made to contact the subject’s LAR to obtain consent, or, if no LAR is available, a family member to provide an opportunity to object to the subject’s enrollment in the study, both before and after the test article is administered;
- A description of the way(s) in which an individual may express his/her desire not to participate and avoid involvement as a subject in the research (e.g., opt-out mechanisms), if any will be made available;
- Reasons why community input is important;
- Known community perceptions/concerns associated with the study, product, and/or standard of care; and
- Identification of individuals to contact for more information about the study.

Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research

FDA interprets the term “public disclosure” to mean dissemination of information (i.e., one-way communication) to the community(ies), the public, and researchers about the emergency research. Appropriate disclosure includes:

- A summary of the research protocol, study design and a description of the procedures to be followed, including identification of any procedures which are experimental;
- A summary of other available treatment options and what is known about their risks and benefits;
- An estimate of how long the study will last and expected duration of the subject’s participation;
- How potential study subjects will be identified;
- Information about the test article’s use, including a balanced description of the risks and expected benefits and any relevant information that is known about adverse events;
- A clear statement that informed consent will not be obtained for most research subjects;
- The rationale as to why the study must be conducted using an exception from informed consent;
- A copy of the informed consent document;
- A description of the attempts that will be made to contact the subject’s LAR to obtain consent, or, if no LAR is available, a family member to provide an opportunity to object to the subject’s enrollment in the study, both before and after the test article is administered;
- A description of the way(s) in which an individual may express his/her desire not to participate and avoid involvement as a subject in the research (e.g., opt-out mechanisms), if any will be made available;
- Reasons why community input is important;
- Known community perceptions/concerns associated with the study, product, and/or standard of care; and
- Identification of individuals to contact for more information about the study.

Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research

The information disclosed should provide sufficient detail to allow a clear understanding of the study design and its results, both positive and negative, including:

- Information about the primary outcome(s) of the study;
- Information about the number and nature of adverse events associated with the test article;
- Whether the study was terminated, and the basis for that decision.

Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research

Before making this determination the IRB should defer the research to allow the plans for community consultation and public disclosure to take place. The IRB should determine whether meaningful feedback was secured from the community and consider the concerns and objections raised. Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research

"Family member" means any one of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship. 45 CFR §46 Waiver of informed consent requirements in certain emergency research and 21 CFR §50.24(m)

If the IRB determines that it cannot approve FDA-regulated research because the research does not meet the above criteria or because other relevant ethical concerns, the IRB must document its findings and provide these findings promptly (no longer than within 30 days) in writing to the investigator and to the sponsor. 21 CFR §50.24(e)